WHAT WE CLAIM IS:

1. A composition that contains a pharmacologically effective amount of at least one BK channel antagonist compound containing the moiety shown in structure (I):

STRUCTURE (I)

or derivatives thereof.

- 2. A composition as claimed in claim 1 wherein the derivatives of structure (I) are selected from the group consisting of: salts, analogues, isomers, and combinations thereof.
- 3. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is selected from the group consisting of: lolitrem B, lolitrem A, lolitrem F, 31-epilolitrem B, lolitrem E, lolitrem E acetate, lolitrem L, lolitrem G, lolitrem C, lolitrem M, lolitriol, lolitriol acetate, lolitrem N, lolitrem J, lolitrem H, lolitrem K, lolicine A and B, 30-desoxy lolitrem B-30α-ol, 30-desoxy-31-epilolitrem B-30α-ol, 30-desoxylolitrem B-30-ene lolilline and combinations thereof.
- 4. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (II):

STRUCTURE (II)

which includes compounds selected from the group consisting of: lolitrem B = 31α , 35β stereochemistry; 31-epilolitrem B = 31β , 35β stereochemistry; lolitrem F = 31α , 35α ; 31-epilolitrem F = 31β , 35α .

5. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (III):

STRUCTURE (III)

which includes compounds selected from the group consisting of: lolitrem E = 31α , 35β stereochemistry where R = H or acetate; lolitrem L = 31α , 35α stereochemistry where R = H or acetate.

WO 2005/016337 PCT/NZ2004/000184

6. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (IV):

STRUCTURE (IV)

which includes compounds selected from the group consisting of: lolitrem A = 31α , 35β stereochemistry; lolitrem G = 31α , 35α stereochemistry.

7. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (V):

STRUCTURE (V)

which includes compounds selected from the group consisting of: lolitriol; = 31α , 35β stereochemistry where R_1 = H or acetate and R_2 = H; lolitrem N = 31α , 35α stereochemistry where R_1 =H or acetate and R_2 =H; Lolitrem J = 31α , 35β stereochemistry where R_1 = H or acetate and R_2 = acetate.

8. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (VI):

STRUCTURE (VI)

which includes lolitrem H = 31α , 35β stereochemistry where R = H or acetate.

9. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (VII):

STRUCTURE (VII)

which includes lolitrem K = 31α , 35β stereochemistry, where R = H or acetate.

10. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (VIII):

STRUCTURE (VIII)

which includes Iolilline = 31α , 35β stereochemistry.

39

11. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (IX):

STRUCTURE (IX)

which includes lolitrem $M = 31\alpha$, 35β stereochemistry.

12. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (X):

STRUCTURE (X)

which includes lolicine $A = 31\alpha$, 35β stereochemistry.

40

13. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (XI):

STRUCTURE (XI)

which includes lolicine B = 31α , 35β stereochemistry.

14. A composition as claimed in claim 1 or claim 2 wherein the antagonist compound is structure (XII):

STRUCTURE (XII)

WO 2005/016337

which includes compounds selected from the group consisting of: 30-desoxylolitrem B-30 α -ol = 31 α , 35 β stereochemistry; 30-desoxy-31-epilolitrem B-30 α -ol = 31 β , 35 β stereochemistry.

15. A composition that contains a pharmacologically effective amount of at least one BK channel antagonist compound wherein the antagonist compound is structure (XIII):

STRUCTURE (XIII)

which includes 30-desoxylolitrem B-30-ene = 35β stereochemistry.

- 16. A composition as claimed in any of the above claims wherein the composition further includes pharmaceutically and physiologically acceptable carriers.
- 17. A composition as claimed in claim 16 wherein the pharmaceutically and physiologically acceptable carriers include components selected from the group including; fillers; excipients; modifiers; humectants; stabilisers; emulsifiers; diluents; and other formulation components such as a use of a lipid vehicle.
- 18. A composition as claimed in any of the above claims wherein the composition is administered in a form selected from the group including: an injection; a tablet; a capsule; a suppository; an injection; a suspension; a drink or tonic; a syrup; a

powder; an ingredient in solid or liquid foods; a nasal spray; a sublingual wafer; a transdermal patch; a transdermal injection; and combinations thereof.

- 19. A composition as claimed in any of the above claims wherein the BK channel antagonist compound or compounds are extracted from endophyte-infected plants and seeds.
- 20. A composition as claimed in any of claims 1 to 18 wherein the BK channel antagonist compound or compounds are extracted from fungal cultures.
- 21 A composition as claimed in any of claims 1 to 18 wherein the BK channel antagonist compound or compounds are derived by chemical synthesis.
- 22. A composition as claimed in any of claims 1 to 18 wherein the BK channel antagonist compound or compounds are extracted from heterologous expression systems including but not limited to bacteria, yeast, fungi, plants and animal cells.
- 23. A composition as claimed in claim 19 wherein the perennial ryegrass seed is from *Lolium perenne*.
- 24. A composition as claimed in any of the above claims wherein the BK channel antagonist compound or compounds has activity against both alpha (α) subunit and alpha plus beta (β) accessory subunit (β_1 to β_4) channels.
- 25. A composition as claimed in any of claims 1 to 4 wherein, for lolitrem B, the degree of antagonist inhibition is approximately 97% for a composition containing approximately 20nM lolitrem B.
- 26. A composition as claimed in any of claims 1 to 4 wherein, for lolitrem B, the half maximal degree of antagonist inhibition (IC₅₀) is found for a composition containing approximately 3.7 ± 0.4 nM of lolitrem B.
- 27. A composition as claimed in any of claims 1 to 3 or 7 wherein, for lolitriol, the

degree of antagonist inhibition is approximately 100% for a composition containing approximately 1000 nM lolitriol.

- 28. A composition as claimed in any of claims 1 to 3 or 7 wherein, for lolitriol, the half maximal degree of antagonist inhibition (IC₅₀) is found for a composition containing approximately 195 nM of lolitriol to inhibit α and β_1 BK channel activity
- 29. A composition as claimed in any of claims 1 to 3 or 7 wherein, for lolitriol, the half maximal degree of antagonist inhibition (IC₅₀) is found for a composition containing approximately 536 \pm 16 nM of lolitriol to inhibit α and β_4 activity.
- 30. A composition as claimed in any of claims 1 to 4 wherein, for 31-epilolitrem B, the degree of antagonist inhibition is approximately 100% for a composition containing approximately 200nM 31-epilolitrem B.
- 31. A composition as claimed in any of claims 1 to 4 wherein, for 31-epilolitrem B, the half maximal degree of antagonist inhibition (IC₅₀) is found for a composition containing approximately 58 ± 6 nM of 31-epilolitrem B to inhibit α and β_1 activity.
- 32. A composition as claimed in any of claims 1 to 4 wherein, for 31-epilolitrem B, the half maximal degree of antagonist inhibition (IC₅₀) is found for a composition containing approximately 49 nM of 31-epilolitrem B to inhibit α and β_4 activity.
- 33. A composition as claimed in any of claims 1 to 4 wherein, for lolitrem E, the degree of antagonist inhibition is approximately 100% for a composition containing approximately 100 nM lolitrem E.
- 34. A composition as claimed in any of claims 1 to 4 wherein the antagonist effect of the composition is not able to be reversed by wash out for concentrations of 10 nM or greater of lolitrem B compound.
- 35. A method of preventing repolarisation or hyperpolarisation of a cell, wherein the

WO 2005/016337 PCT/NZ2004/000184

44

cell contains a BK channel, including the administration to the cell of a pharmacologically effective amount of composition containing a BK channel antagonist as claimed in any of claims 1 to 34.

36. Use of a composition as claimed in any of claims 1 to 34 for preventing repolarisation or hyperpolarisation of a cell, wherein the cell contains a BK channel.